

~~REPLACED~~  
WE CLAIM: ~~ART 34 AMDT~~

- 1) A method of modifying a target nucleic acid of interest at a target locus within a genome of a host comprising:
  - 5 a) introducing into the host a gene targeting construct (GTC) and culturing the host so as to:
    - i) express the gene targeting construct encoding a gene targeting RNA, to produce the gene targeting message RNA capable of priming reverse transcription by a reverse transcriptase (RT);
    - 10 ii) reverse transcribe at least a portion of the gene targeting message RNA to produce an *in vivo* gene targeting substrate (GTS) having a gene targeting nucleotide sequence (GTNS), wherein the GTNS is homologous to the target locus and comprises a sequence modification compared to the target nucleic acid; and,
  - 15 b) selecting a host having the sequence modification at the target locus.
- 2) The method of claim 1, wherein the host is capable of expressing the RT prior to transforming the host with the gene targeting construct.
- 20 3) The method of claim 1, wherein the host is modified to be capable of expressing the RT at the same time as, or after, transforming the host with the gene targeting construct.
- 25 4) The method of claim 1, 2 or 3, wherein the GTC is introduced into the host by transformation, by cross breeding or by cell fusion.
- 30 5) A gene targeting construct comprised of recombinant nucleic acid sequences in a host having a host genome, wherein the gene targeting construct encodes and is capable of expressing a gene targeting message RNA, wherein the gene targeting message RNA is capable of self-priming reverse transcription by a reverse transcriptase in the host to produce a gene targeting substrate having a gene targeting nucleotide sequence,